

*Citation for published version:*

Tillett, W, Shaddick, G, Jobling, A, Askari, A, Cooper, A, Creamer, P, Clunie, G, Helliwell, PS, James, J, Kay, L, Korendowych, E, Lane, S, Packham, J, Shaban, R, Thomas, ML, Williamson, L & McHugh, N 2017, 'Effect of anti-TNF and conventional synthetic disease-modifying anti-rheumatic drug treatment on work disability and clinical outcome in a multicentre observational cohort study of psoriatic arthritis', *Rheumatology*, vol. 56, no. 4, pp. 603-612. <https://doi.org/10.1093/rheumatology/kew433>

*DOI:*

[10.1093/rheumatology/kew433](https://doi.org/10.1093/rheumatology/kew433)

*Publication date:*

2017

*Document Version*

Peer reviewed version

[Link to publication](https://doi.org/10.1093/rheumatology/kew433)

This is a pre-copyedited, author-produced version of an article accepted for publication in *Rheumatology* following peer review. The version of record Tillett, W., Shaddick, G., Jobling, A., Askari, A., Cooper, A., Creamer, P., ... McHugh, N. (2016). Effect of anti-TNF and conventional synthetic disease-modifying anti-rheumatic drug treatment on work disability and clinical outcome in a multicentre observational cohort study of psoriatic arthritis. *Rheumatology* is available online at: <https://doi.org/10.1093/rheumatology/kew433>.

## University of Bath

### Alternative formats

If you require this document in an alternative format, please contact:  
[openaccess@bath.ac.uk](mailto:openaccess@bath.ac.uk)

#### General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

#### Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Effect of anti-TNF and csDMARD treatment on work disability and clinical outcome  
in a multicentre observational cohort study of psoriatic arthritis

William Tillet<sup>1,12</sup>, Gavin Shaddick<sup>2</sup>, Amelia Jobling<sup>2</sup>, Ayman Askari<sup>3</sup>, Annie Cooper<sup>4</sup>,  
Paul Creamer<sup>5</sup>, Gavin Clunie<sup>6</sup>, Philip S. Helliwell<sup>7</sup>, Jana James<sup>1</sup>, Lesley Kay<sup>8</sup>, Eleanor  
Korendowych<sup>1</sup>, Suzanne Lane<sup>9</sup>, Jonathon Packham<sup>10</sup>, Ragai Shaban<sup>4</sup>, Matthew L.  
Thomas<sup>2</sup>, Lyn Williamson<sup>11</sup> and Neil McHugh<sup>1,12</sup>,

<sup>1</sup>Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom,

<sup>2</sup>University of Bath, Department of Mathematics, Bath, United Kingdom,

<sup>3</sup>Robert Jones and Agnes Hunt Hospital, Shropshire, United Kingdom,

<sup>4</sup>Queen Alexandra Hospital, Portsmouth, United Kingdom,-

<sup>5</sup>North Bristol NHS foundation trust, Bristol, United Kingdom,

<sup>6</sup>Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom,

<sup>7</sup>NIHR Leeds Biomedical Research Unit, University of Leeds and Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom,

<sup>8</sup>Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, United Kingdom,

<sup>9</sup>Ipswich Hospital NHS Trust, Ipswich, United Kingdom,

<sup>10</sup>Haywood Rheumatology Centre, Stoke-on-Trent, United Kingdom,

<sup>11</sup>Great Western Hospitals NHS Foundation Trust, Swindon, United Kingdom

<sup>12</sup> University of Bath, Department of pharmacy and pharmacology, Bath, United Kingdom.

[w.tillett@nhs.net](mailto:w.tillett@nhs.net)

Royal National Hospital for Rheumatic Diseases

Upper Borough Walls

Bath, UK

Tel: +44 (0)1225448444

Mobile: +44 (0)7980960722

Fax: +44 (0)1225336809

**MeSH terms:** Psoriatic Arthritis, Outcomes Research, csDMARDS, anti-TNF, Work  
Disability,

**Short title:** Work Disability in Psoriatic Arthritis

**Word count:** 2888 (excluding abstract- 225)

## **ABSTRACT**

**Objective:** To determine the effect of medical treatment on work disability in patients with active psoriatic arthritis, in the real world setting.

**Methods:** Four hundred patients with active psoriatic arthritis commencing or switching to anti-TNF or conventional synthetic disease modifying anti rheumatic drugs (csDMARD) were recruited to a prospective, UK, multicentre, observational cohort study. Work disability was measured using the work productivity and activity- specific health problem (WPAI-SHP) instrument and peripheral joint activity with the Disease Activity in Psoriatic Arthritis (DAPSA) composite measure.

**Results:** Four hundred patients were recruited of whom 229 (57.25%) were working (of any age). Sixty two patients of working age (24%) were unemployed. At six months there was a 10% improvement in presenteeism ( $p=0.007$ ) and 15% improvement in work productivity ( $p=0.001$ ) amongst working patients commenced on csDMARDs ( $n=164$ ) versus a larger and more rapid 30% improvement in presenteeism ( $p<0.001$ ) and 40% improvement in work productivity ( $p<0.001$ ) amongst those commenced on anti-TNF ( $n=65$ ). Clinical response was poor amongst patients commenced on a csDMARD ( $n=272$ ) with 8.4 point improvement in DAPSA ( $p<0.001$ ) versus those commenced on anti-TNF ( $n=121$ ) who had a 36.8 point improvement ( $p<0.001$ ).

**Conclusion:** We report significant and clinically meaningful improvements in both work disability and clinical outcomes after commencement of anti-TNF in the real world setting. Improvements in all outcomes amongst those commencing csDMARDS were slower and of smaller magnitude.

## INTRODUCTION

Prospective cohort studies have demonstrated progressive joint damage, reduced quality of life and high levels of disability in patients with Psoriatic Arthritis (PsA).[1-4] There is growing evidence to indicate that early diagnosis and treatment can ameliorate disease activity, reduce joint damage and prevent disability.[5-8]

There is increasing recognition by clinicians, patient groups and regulatory agencies of the importance of measuring the effect of treatment with 'real world' outcomes important to patients, thereby capturing all the ways in which disease affects the individual.[9, 10] When assessing the effect of treatment, outcome measures such as joint counts or biomarkers may not capture all aspects of disease and may even be discordant with patient reported outcomes, and as a result, fail to capture important benefits to patients.[11] Work disability has become a particularly important outcome in the evaluation of chronic inflammatory rheumatic disease.[12, 13] Work disability was ranked as a highly important outcome by patients in the European League Against Rheumatism (EULAR) led Psoriatic Arthritis Impact of Disease (PsAID) study.[14] The PsAID was developed specifically for use in PsA as a patient centred, patient reported outcome of impact of disease to capture all the ways in which PsA affects an individual. Patients ranked impacts of disease in order of importance and work was ranked 4<sup>th</sup> behind pain, skin and fatigue.[14]

There are high rates of work disability in psoriatic arthritis. Estimates of unemployment and work disability range from 20-50% and 16-39% respectively in clinical trials and cohort studies.[3] Presenteeism (reduced effectiveness at work) and productivity loss (presenteeism plus absenteeism) have been shown to be primarily associated with

disease activity in psoriatic arthritis raising the possibility that amelioration of active disease may lead to reduced work disability. [15]

In the present study we set out to assess the effect of medical treatment on work disability in patients with active psoriatic arthritis, in an unselected population of patients undergoing a change in medication as part of routine clinical practice in the UK.

## METHODS

The study design for Long Term Outcomes in Psoriatic Arthritis II (LOPAS II) has previously been reported.[15] In brief, LOPAS II is a prospective, multicentre observational cohort study to investigate work disability in PsA and the effect of treatment. Twenty-three sites across the UK participated in the study (Supplementary figure 1). Four hundred patients of any age and disease duration who fulfilled the classification for psoriatic arthritis (CASPAR) criteria[16] and were being commenced on conventional synthetic Disease Modifying Anti Rheumatic Drugs (csDMARD) or anti-Tumour Necrosis Factor inhibitors (anti-TNF) as part of routine clinical care were recruited. Any patients commencing csDMARD or anti-TNF were eligible for inclusion including new monotherapy, combination treatment and switching agents. The sample size was calculated to achieve 80% power to detect the minimal clinically important difference of 7%[17] change in presenteeism at 5% level of significance. Patients under 18 years and non-English speaking were excluded. Physician and patient reported outcome measures were collected at routine clinic appointments baseline, 3 and 6 months with additional patient reported outcomes only by post at weeks 2 and 4. Study recruitment occurred between September 2011 and April 2013.

Work disability was assessed with the work productivity and activity impairment questionnaire (WPAI) [18]. The WPAI is a six item patient reported questionnaire asking patients to report the degree to which they experience difficulty at work due to a specific health problem, in this case PsA over the preceding week. Four outcomes can be generated from the WPAI, expressed in percentages:

- % Absenteeism (absence from work),
- % Presenteeism (reduced effectiveness at work),
- % Productivity loss (a function of both absenteeism and presenteeism)
- % General activity impairment attributable to a specific health problem.

The WPAI has been validated for use in rheumatoid arthritis and ankylosing spondylitis and the presenteeism measure by Outcome Measures in Rheumatology (OMERACT).[19-21] Peripheral joint disease activity was measured using the composite Disease Activity in Psoriatic Arthritis (DAPSA) score, a summation of 66 swollen and 68 tender joint count, C-reactive protein (CRP), patient global and pain visual analogue scores (VAS).[22] Patient reported outcomes included physical function with the health assessment questionnaire (HAQ), the European quality of life five domain questionnaire (EQ5D), dermatology quality of life index (DLQI), Functional Assessment of Chronic Illness Therapy Fatigue scale (FACIT), and global/domain specific activity VAS scores.

This study is reported in accordance with the ‘strengthening the reporting of observational studies in epidemiology’ (STROBE) guidelines for the reporting of cohort studies.[23]

### *Statistical Analysis*

All analysis was performed using the statistical package R 2014.[24] Univariate comparisons between treatment groups at baseline were performed using Wilcoxon tests. Difference within groups was made on an intention to treat basis (excluding seven patients who were never issued with a prescription). Multiple imputation, based on both the available data and underlying temporal patterns within responses for each patient, was used to infer values of missing predictor data using the Amelia II package in R.[25] Changes in the responses over time are presented as plots of mean values by time point. Regression modelling was used to model rates of improvements using actual dates (rather than planned time points) and the effects of potential predictor variables.

Rates of improvement, using actual dates rather than planned time points, were modeled using regression models with missing values in explanatory variables estimated using multiple imputation. P values for significance tests of potential differences between rates of improvement in different groups, defined by either by treatment or duration of disease, are obtained from including interaction terms to these regression models. WPAI response variables were recorded in (or categorised to) groups representing deciles and multivariate Poisson regression models used to formally assess changes over time. Differences in rates of improvements were assessed allowing for age, sex, disease duration, baseline HAQ, DAPSA and EQ5D. To allow for the expected excess of zeros in the response variables, zero-inflated Poisson (ZIP) models were used, with a consistent set of covariates used for both the Binomial and Poisson components of the model.

### **RESULTS**

The mean age of patients was 46.8 years (sd 11.02), mean disease duration 5.8 years (sd 8.00), and 49.9% were female. Two hundred and twenty six patients of working

age patients (64%) were in work with a further ten over retirement age still working. Ninety two patients of working age (26%) were unemployed. Table 1 illustrates the baseline characteristics of all patients who were commenced on anti-TNF and DMARD. A supplementary file (supplementary table 1) compares baseline characteristics of working age employed and unemployed patients at baseline. Unemployed patients had worse physical function than those who were employed (HAQ 1.5 and 0.88 respectively,  $p<0.001$ ) and worse quality of life (EQ5D 0.71 and 0.78 respectively  $p<0.001$ ).

#### *Follow up time points and loss to follow up*

Seven of the 400 patients recruited did not commence a drug and were excluded from the analysis. A total of 63 patients did not complete six months follow up. Forty nine patients became lost to follow up and a further 14 withdrew from the study (two became pregnant, two developed cancer, one relocated, nine cited personal reasons), two patients had their diagnosis changed to osteoarthritis and one patient died of an unrelated condition during the six months. Figure 1 illustrates the study recruitment and follow up, by treatment group and those included in the work analysis. There were no statistically significant differences in demographic or baseline disease characteristics between those lost to follow up and those who remained in the study.

#### *Drugs commenced during LOPAS II*

Of the 272 patients who started (including switching and step-up combination treatment) csDMARDS 54% started methotrexate, 30% Sulphasalazine, 12% Leflunomide, 1% commenced Cyclosporine, 1% Azathioprine, 1% Hydroxychloroquine and 1% combination treatment. Of the 121 who commenced anti-TNF (including switching and step-up combination treatment) 56% commenced



Adalimumab, 35% Etanercept, 5% Infliximab and 4% Golimumab. The planned study clinical follow up was 'per routine care' with clinical assessment at 3 and 6 months. Additional patient reported questionnaires were completed at 2 and 4 weeks by post. There was variation in the times at which patients were seen; median and IQRs for days from baseline for the five time points were 14 (14-26), 28 (28-42), 98 (89-119), 196 (179-224).

#### *Work Disability and Clinical Outcome*

One hundred and sixty four of the 272 patients commenced on csDMARD and 65 of the 121 commenced on anti-TNF were working (figure 1). Over six months follow up those commenced on csDMARDS had a 10% improvement in presenteeism (IQR 30-20  $p=0.007$ ) and 15% improvement in productivity loss (IQR 40 to 25  $p=0.001$ ). Patients commenced on anti-TNF had a 30% improvement in presenteeism (IQR 40 to 10  $p<0.001$ ) and 40% improvement in productivity loss (IQR 50 to 10  $p<0.001$ ). Improvement was more rapid and of a greater magnitude amongst those commenced on anti-TNF (Figure 2). Although absenteeism did improve this improvement was not statistically significant.

Clinical improvement was measured using the DAPSA composite index. Patients commenced on csDMARD had 8.4 point improvement (IQR 38.6 - 30.2,  $p<0.0001$ ). Patients commenced on anti-TNF had a 36.8 point improvement (IQR 50.8 to 14.0) (Figure 3). Sixty five percent of those commencing anti-TNF achieved a 50% response in DAPSA versus 26% of those commencing csDMARD. Tables 2 and 3 summarise the individual changes in patient reported and clinical outcome during the course of six months follow up. Patients commenced on anti-TNF had achieved improvements in all

outcomes and these improvements exceed the minimally important difference (MID) in global activity[26], pain[26], physical function (HAQ)[26], fatigue (FACIT)[27] and quality of life (EQ5D)[28] but not skin specific quality of life (DLQI)[29]. Smaller, but statistically significant improvements were observed amongst patients commenced on csDMARDS although improvements greater than the MID were only observed in global activity, pain, and fatigue. Change in global, pain, joint and skin specific VAS, HAQ, DAPSA, FACIT and DLQI amongst both groups are illustrated in Figure 3.

A sub-analysis was performed to investigate whether the greater change seen in patients receiving anti-TNF versus csDMARD might be sensitive to baseline disease activity. Those starting on anti-TNF have higher disease activity and therefore may have greater scope for improvement. It was found that the rate of improvement of presenteeism, productivity loss and activity impairment in anti-TNF versus DMARD treatment was seen in patients with both high and low baseline disease activity. Rates of improvement in absenteeism were slower amongst those with low disease activity.

#### *Work Disability –rates of change during follow up*

Given the observational nature of the study there was variance in follow up around each planned follow up time point. In order to assess differences in rate of change over time analyses were undertaken by exact time point (days). Significant decreases were found in all WPAI domains (absenteeism, presenteeism, productivity loss and activity impairment) during follow up ( $p < 0.0001$ ). Patients commenced on anti-TNF improved more rapidly than those on csDMARDS in all WPAI domains ( $p < 0.001$  for differences in rate of improvement).

### *Work disability and disease duration*

Two hundred and ninety-two patients had complete recorded data for onset of disease, with 83 patients recorded as having disease duration  $\leq 2$  years and 209 greater than 2 years at baseline. Previously identified clinical and demographic predictor variables were included in the regression including age, disease duration, global and joint VAS scores, HAQ and employer helpfulness. [15] Patients with shorter duration had significantly higher activity loss ( $p=0.002$ ), presenteeism ( $p=0.003$ ), absenteeism ( $p<0.001$ ) and productivity loss ( $p=0.008$ ) at baseline. There was a statistically greater improvement in productivity loss amongst those with disease duration  $<2$  years,

## DISCUSSION

We report improvement in work disability, clinical and patient reported outcome amongst a cohort of patients in the UK commenced on anti-TNF and csDMARDs, for active psoriatic arthritis, as part of their routine care. Improvements in all outcomes were more rapid and of greater magnitude amongst those commenced on anti-TNF despite higher levels of baseline disease activity. Notably, gain in work productivity with anti-TNF was even greater with shorter duration disease. Clinical and patient reported outcome response to csDMARDs was poor, achieving MID improvements in pain/global VAS and fatigue alone. To our knowledge LOPAS II is the first study of its type, sufficiently powered to use work disability as the primary endpoint.

There has been interest in the effect of treatment on work disability in long term rheumatic diseases, in particular studies comparing different classes of drug treatment. Many of the recent randomised controlled trials (RCT's) of novel therapeutic agents in psoriatic arthritis have included work as a secondary endpoint. [30-32] Comparison of

biological and conventional synthetic disease modifying anti-rheumatic drugs in rheumatoid arthritis have demonstrated reduced absenteeism, reduced sick leave, higher employment potential and greater levels of employment potential amongst those treated with biologics.[33] The data we present in this present study describes the differential effect of anti-TNF and csDMARDs on patient reported work disability (presenteeism and productivity loss) in a well classified group of patients with psoriatic arthritis in the real world setting. The work disability data we report is attributable to psoriatic arthritis (using the WPAI-SHP) and is granular (over the last week) minimising recall bias. The study is further strengthened by using well defined patients (CASPAR criteria), multicentre recruitment across the UK, and broad inclusion criteria (encompassing patients of any age and disease duration) which increase the generalisability of the findings.

Whilst there is recognition that work is an important outcome there has been debate on how to use the measure and interpret work data. It has been argued that there are too many contextual factors to justify wider uptake of work as a disease outcome measure. Recognising these concerns the Outcome Measures in Rheumatology (OMERACT) core set of domains for psoriatic arthritis controlled trials and observational studies placed participation (including work) in the outer circle for further research in 2007.[34] The findings of this study support the view that contextual factors may have less impact in the context of active disease than previously thought, particularly with respect to measures of in work disability.[33] We have previously reported that measures of reduced effectiveness at work (presenteeism and productivity loss) are more strongly associated with disease activity than disease severity (damage) or contextual measures.[15] Work disability has also been found to be associated with fatigue in

PsA.[35] Now, in this present study, as in the highly selected populations of novel biologic agent RCT's, we have observed that work disability improves in parallel to clinical disease activity despite contextual factors. The finding that disease duration of <2 years is associated with more rapid improvement is of clinical interest, particularly because unemployment is often irreversible, and this may add to the building case for early intervention in newly diagnosed psoriatic arthritis. Our results support the role for work disability as an effective, patient centred disease outcome measure of participation.

The clinical improvement seen after commencing anti-TNF and relative lack of response amongst csDMARDS in this study is striking. The effectiveness of anti-TNF in PsA is well established whereas studies of csDMARD are limited.[36] Many of the csDMARD studies were conducted before the modern era of more aggressive treatment with higher doses, combination therapy and a treat to target approach. The results of this observational cohort study has shown that amongst 272 patients commenced on csDMARDs, as part of routine care, improvement in clinical, biochemical and patient reported measures was slow of small magnitude. As this was an observational study we did not influence csDMARD choice or dosing and it is possible that some of the poor response may be related to lower dosing, differing dose escalation regimes and inclusion of drugs that may be less efficacious in PsA. Finally we should also note there is also an ongoing trend to improvement in the csDMARD group (Figure 3) which may become significant with longer follow up.

When interpreting the findings of this study is important to highlight certain methodological limitations. LOPAS II was an observational study therefore direct

comparison cannot be made between treatment groups. Patients were recruited at a point of high disease activity therefore some improvement over the course of the study may be related to the natural relapsing remitting course of disease. It is our view this effect will have been small, firstly as patients commencing anti-TNF were in sustained flare (as part of their eligibility for anti-TNF in the National Health Service, having failed csDMARDS) and secondly the limited improvement seen amongst those commenced on csDMARDS. Finally it is important to recognise that the DAPSA is a measure of articular disease in PsA, rather than a composite outcome measure capturing all domains of disease. The DAPSA will not capture other important domains of disease (enthesitis, skin, dactylitis, axial involvement) except indirectly through the global VAS score.

In conclusion we report data from a large observational cohort study on the effect of medical treatment with anti-TNF or csDMARDS commenced as part of routine care on patient reported work disability and clinical outcome. Work disability and clinical outcome improved quickly to clinically significant levels amongst those commenced on anti-TNF despite high levels of disease activity. Improvements in work disability occurred more slowly and were of a smaller magnitude and clinical improvement was poor amongst those commenced on csDMARDS. This data supports the view that work disability is reversible with effective treatment of active disease in the real world setting.

## KEY MESSAGES

1. Work disability in active Psoriatic Arthritis is reversible with medical treatment

2. Clinically meaningful improvements in both work disability and clinical outcomes after commencement of anti-TNF.
3. Improvements in all outcomes amongst those commencing csDMARDS were slower and of smaller magnitude.

## ACKNOWLEDGEMENTS

We would like to thank the patients for their participation in this research project. We would also like to thank all the Principle Investigators in LOPAS II: Dr Gavin Clunie Dr Gerald George, Dr Richard Haigh , Dr Adrian Jones, Dr Stuart Kyle, Mrs Dawn Simmons, Dr Richard Smith, Prof Paul Thomson, Mrs Barbara Williams-Yesson and their research teams. We would like to thank Nicola Waldron, nurse specialist in psoriatic arthritis, Charlotte Cavill our database manager and Mandy Knight and Austin Smith our database administrators.

### **Funding:**

This study was funded through an unrestricted grant from Abbvie laboratories ltd and is supported through the National Institute for Health research (NIHR).

### **Disclosure:**

LJK is a Generation Q Fellow with the Health Foundation. GS, MJ, AA, AC, PC, GC, PSH, JJ, EK, SL, JP, RS, MLT, LW, NMC declare no conflicts of interest relating to this manuscript.

### **Ethical Approval:**

This study (LOPAS II) was approved by the South Wales Research Ethics Committee Panel D. All patients signed written consent in accordance with the declaration of Helsinki



## REFERENCES

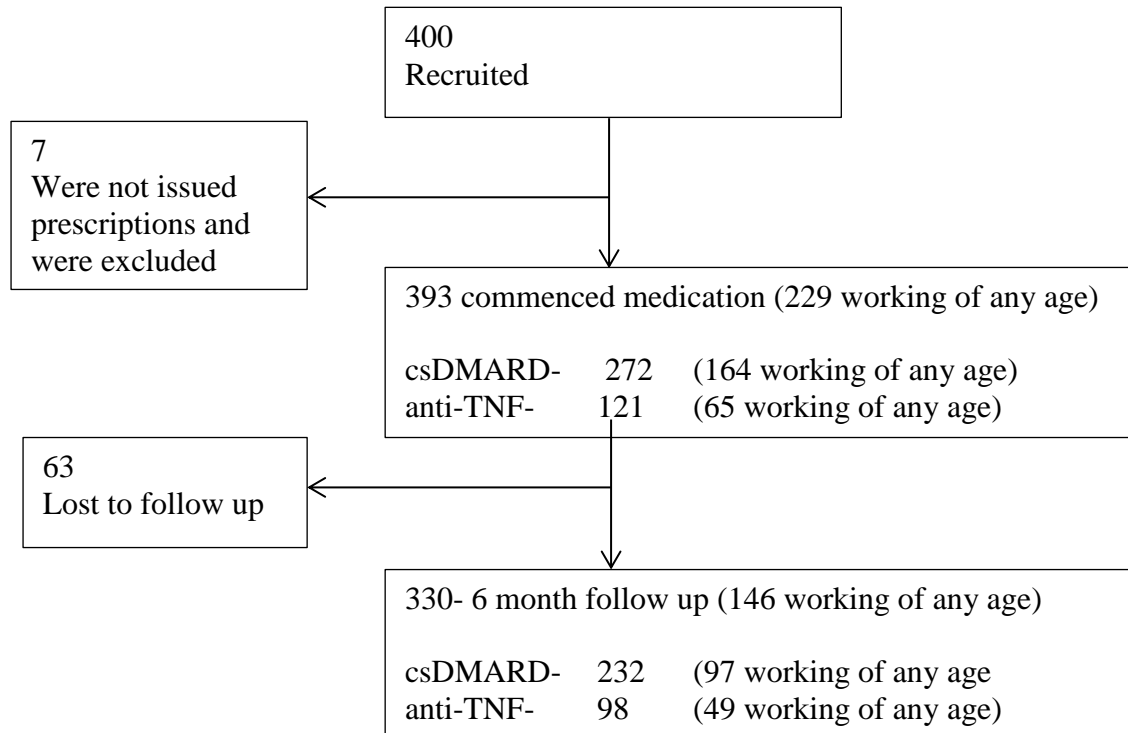
1. Gladman DD, Stafford-Brady F, Chang CH, Lewandowski K, Russell ML. Longitudinal study of clinical and radiological progression in psoriatic arthritis. *J Rheumatol*. 1990;17(6):809-12. Epub 1990/06/01.
2. McHugh NJ, Balachrishnan C, Jones SM. Progression of peripheral joint disease in psoriatic arthritis: a 5-yr prospective study. *Rheumatology (Oxford)*. 2003;42(6):778-83. Epub 2003/05/06.
3. Tillett W, de-Vries C, McHugh NJ. Work disability in psoriatic arthritis: a systematic review. *Rheumatology*. 2012;51(2):275-83. Epub 2011/07/15.
4. Torre AJ RP, Arribas CJ, Ballina GJ, Riestra NJ, Lopez LC. Psoriatic arthritis (PA): a clinical, immunological and radiological study of 180 patients. *British journal of rheumatology*. 1991;30(4):245-50.
5. Gladman DD, Thavaneswaran A, Chandran V, Cook RJ. Do patients with psoriatic arthritis who present early fare better than those presenting later in the disease? *Ann Rheum Dis*. 2011;70(12):2152-4. Epub 2011/09/15.
6. Coates L, Moverley A, McParland L, Brown S, Collier H, Brown SR, et al. Effect of tight control of inflammation in early psoriatic arthritis (TICOPA): a multicentre, open-label, randomised controlled trial. *The Lancet*. 2014;383:S36.
7. Tillett W, Jadon D, Shaddick G, Cavill C, Korendowych E, de Vries CS, et al. Smoking and delay to diagnosis are associated with poorer functional outcome in psoriatic arthritis. *Ann Rheum Dis*. 2013;72(8):1358-61. Epub 2013/01/08.
8. Haroon M, Gallagher P, FitzGerald O. Diagnostic delay of more than 6 months contributes to poor radiographic and functional outcome in psoriatic arthritis. *Ann Rheum Dis*. 2015;74(6):1045-50. Epub 2014/02/15.
9. Bojke L, Spackman E, Hinde S, Helliwell P. Capturing all of the costs in NICE appraisals: the impact of inflammatory rheumatic diseases on productivity. *Rheumatology*. 2012;51(2):210-5. Epub 2012/01/24.
10. de Wit M, Abma T, Koelewijn-van Loon M, Collins S, Kirwan J. Involving patient research partners has a significant impact on outcomes research: a responsive evaluation of the international OMERACT conferences. *BMJ open*. 2013;3(5). Epub 2013/05/15.
11. Dandorfer SW, Rech J, Manger B, Schett G, Englbrecht M. Differences in the patient's and the physician's perspective of disease in psoriatic arthritis. *Semin Arthritis Rheum*. 2012;42(1):32-41. Epub 2012/03/20.
12. Black CM. Sickness absence and musculoskeletal disorders. *Rheumatology (Oxford)*. 2012;51(2):204-5. Epub 2012/01/24.
13. Short P, Jones AC, Walker D, Kavanaugh A, Moots RJ. Working at arthritis. *Rheumatology (Oxford)*. 2012;51(2):201-3. Epub 2011/12/20.
14. Rivers TM, Tillett WS. Studies on Varicella : The Susceptibility of Rabbits to the Virus of Varicella. *The Journal of experimental medicine*. 1923;38(6):673-90. Epub 1923/11/30.
15. Tillett W, Shaddick G, Askari A, Cooper A, Creamer P, Clunie G, et al. Factors influencing work disability in psoriatic arthritis: first results from a large UK multicentre study. *Rheumatology (Oxford)*. 2015;54(1):157-62. Epub 2014/08/16.
16. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum*. 2006;54(8):2665-73. Epub 2006/07/28.

17. Reilly MC BM, Brahant Y, Gerlier L, Tan SC, Sandborn WJ. Defining the minimally important difference for WPAI: CD Scores: What is a relevant impact on work productivity in active Crohn's disease? *Gut*. 2007;56 (Suppl,3):A159.
18. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics*. 1993;4(5):353-65. Epub 1993/10/05.
19. Reilly MC, Gooch KL, Wong RL, Kupper H, van der Heijde D. Validity, reliability and responsiveness of the Work Productivity and Activity Impairment Questionnaire in ankylosing spondylitis. *Rheumatology*. 2010;49(4):812-9. Epub 2010/01/27.
20. Zhang W, Bansback N, Boonen A, Young A, Singh A, Anis AH. Validity of the work productivity and activity impairment questionnaire--general health version in patients with rheumatoid arthritis. *Arthritis Res Ther*. 2010;12(5):R177. Epub 2010/09/24.
21. NIHR. Informed Consent Toolkit. 2016; Available from: <http://www.ct-toolkit.ac.uk/routemap/informed-consent>.
22. Schoels M, Aletaha D, Funovits J, Kavanaugh A, Baker D, Smolen JS. Application of the DAREA/DAPSA score for assessment of disease activity in psoriatic arthritis. *Ann Rheum Dis*. 2010;69(8):1441-7.
23. von Elm E, Altman DG, Egger M, Pocock SJ, Gotsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Annals of internal medicine*. 2007;147(8):573-7. Epub 2007/10/17.
24. R, Core, Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria [Internet]. 2014. Available from: <http://www.R-project.org/>.
25. Honaker J, King G. Amelia II: A Program for Missing Data. . *Journal of Statistical Software*. 2011;45(7):1-47.
26. Kwok T, Pope JE. Minimally important difference for patient-reported outcomes in psoriatic arthritis: Health Assessment Questionnaire and pain, fatigue, and global visual analog scales. *J Rheumatol*. 2010;37(5):1024-8. Epub 2010/03/17.
27. Cella D, Yount S, Sorensen M, Chartash E, Sengupta N, Grober J. Validation of the Functional Assessment of Chronic Illness Therapy Fatigue Scale relative to other instrumentation in patients with rheumatoid arthritis. *J Rheumatol*. 2005;32(5):811-9. Epub 2005/05/04.
28. Walters SJ, Brazier JE. Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation*. 2005;14(6):1523-32. Epub 2005/08/23.
29. Melilli L SR, Thompson C. Minimum clinically important difference in Dermatology Life Quality Index in moderate to severe plaque psoriasis patients treated with adalimumab. . *Journal American Academy Dermatology*. 2006;54(Suppl):AB221.
30. Kavanaugh A, Gladman D, van der Heijde D, Purcaru O, Mease P. Improvements in productivity at paid work and within the household, and increased participation in daily activities after 24 weeks of certolizumab pegol treatment of patients with psoriatic arthritis: results of a phase 3 double-blind randomised placebo-controlled study. *Ann Rheum Dis*. 2015;74(1):44-51. Epub 2014/06/20.
31. Kavanaugh A, Antoni C, Mease P, Gladman D, Yan S, Bala M, et al. Effect of infliximab therapy on employment, time lost from work, and productivity in patients with psoriatic arthritis. *J Rheumatol*. 2006;33(11):2254-9. Epub 2006/09/09.

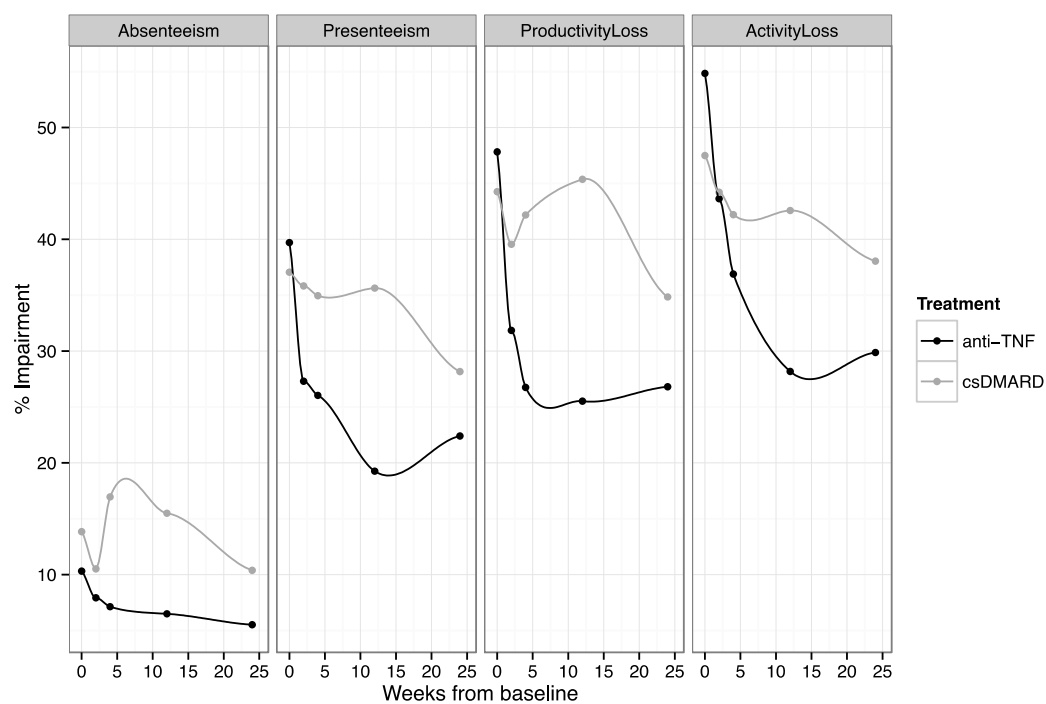
32. Gladman D, Smpalis JS, Martel MJ, Gooch KL, Wong RL, Guerette B. Impact of Adalimumab on Presenteeism for Patients with Psoriatic Arthritis and Reliability and Validity of the Work Limitations Questionnaire: Results of ACCLAIM. *Journal of Rheumatology*. 2009;36(11):2595.
33. Zhang W, Sun H, Emery P, Sato R, Singh A, Freundlich B, et al. Does achieving clinical response prevent work stoppage or work absence among employed patients with early rheumatoid arthritis? *Rheumatology* 2012;51(2):270-4. Epub 2011/07/02.
34. Gladman DD, Mease PJ, Strand V, Healy P, Helliwell PS, Fitzgerald O, et al. Consensus on a core set of domains for psoriatic arthritis. *J Rheumatol*. 2007;34(5):1167-70. Epub 2007/05/05.
35. J B, Anton R, Navarro Ruiz A, Castera M, Jd R, A M. Persistence and Econ" Mic Impact of Etanercept and Adalimumab Dose Reduction In Rheumatoid Arthritis, Psoriatic Arthropathy and Ankylosing Spondylitis Patients With At Least 1 Year In Clinical Remission: Experience From 2 Spanish Teaching Hospitals During 5 Years of Follow-Up. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*. 2015;18(7):A643. Epub 2015/11/05.
36. Ash Z, Gaujoux-Viala C, Gossec L, Hensor EM, Fitzgerald O, Winthrop K, et al. A systematic literature review of drug therapies for the treatment of psoriatic arthritis: current evidence and meta-analysis informing the EULAR recommendations for the management of psoriatic arthritis. *Ann Rheum Dis*. 2011. Epub 2011/08/02.



Figure 1- Loss to follow up during study LOPAS II



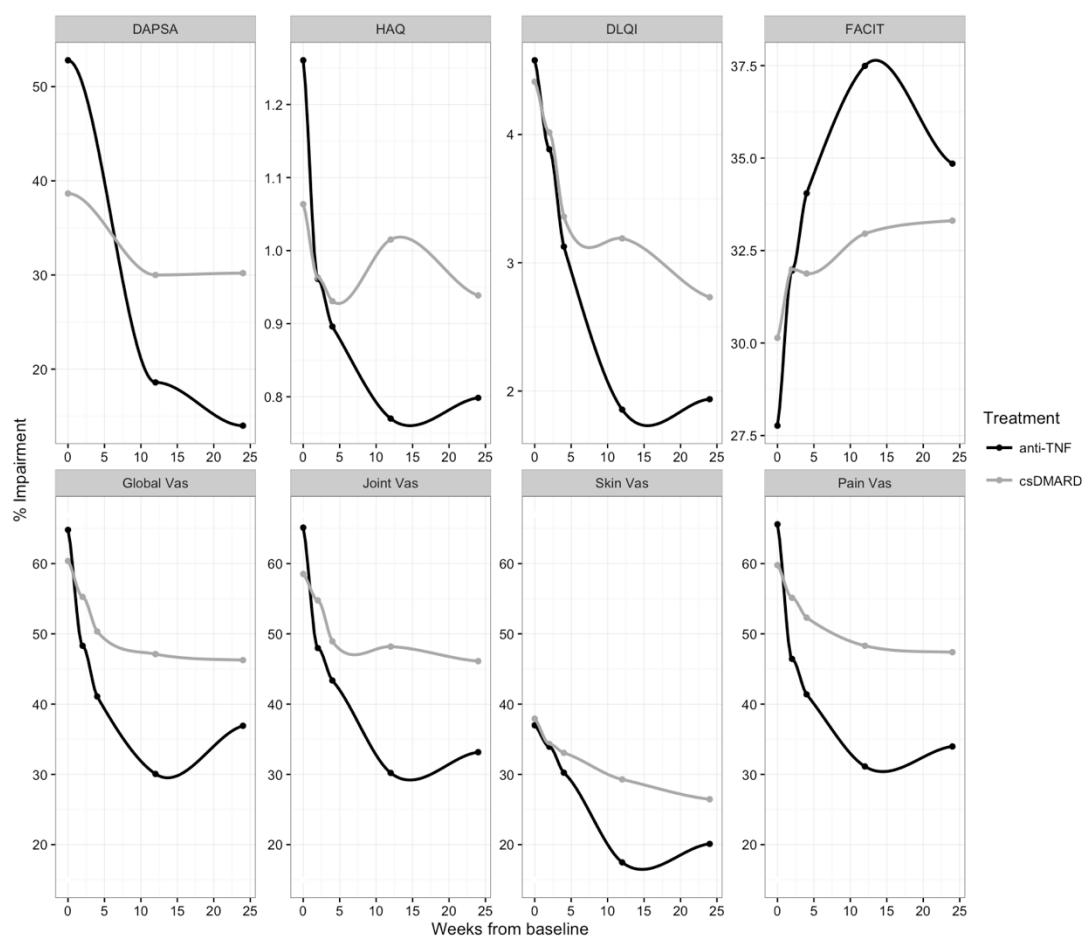




**Figure 2**

**Work outcome amongst working participants commenced on anti-TNF (n=65) and conventional synthetic DMARD (n=164)**

WPAI- Work productivity activity and impairment index  
 csDMARD- conventional synthetic Disease Modifying Anti-Rheumatic Drug  
 anti-TNF- anti-Tumour Necrosis Factor alpha inhibitor



**Figure 3**  
**Clinical outcomes amongst participants commenced on anti-TNF (n=121) and conventional synthetic DMARD (n=272)**

DAPSA- Disease activity in Psoriatic Arthritis  
 HAQ- Heath Assessment Questionnaire  
 DLQI- Dermatology Quality of Life Index  
 FACIT-F- Functional Assessment of Chronic Illness Therapy Fatigue scale  
 VAS- Visual Analogue Scale  
 csDMARD- conventional synthetic Disease Modifying Anti-Rheumatic Drug  
 anti-TNF- anti-Tumour Necrosis Factor alpha inhibitor



| Outcome (range)   | DMARD<br>(median/ IQR) | Anti-TNF<br>(median/ IQR) | P value<br>(Wilcox) |
|---|------------------------|---------------------------|---------------------|
| No. of patients (n)                                     | 272                    | 121                       |                     |
| Percentage Male (%)                                     | 46.7                   | 23.5                      |                     |
| Age   | 50.6 (41.9-60.2)       | 52.8 (42.9-62.3)          | 0.2759              |
| Duration  | 5.0 (2.0-11.0)         | 11.0 (3.5-18.5)           | <b>&lt;0.0001</b>   |
| HAQ (0-1)   | 0.9 (0.5-1.5)          | 1.1 (0.8-1.8)             | <b>0.0116</b>       |
| EQ5D (-0.11-1)  | 0.7 (0.6-0.9)          | 0.7 (0.6-0.8)             | 0.2469              |
| DLQI (0-30)   | 2.0 (1.0-6.0)          | 3.0 (1.0-6.0)             | 0.9685              |
| Pain Vas (0-100)  | 62.0 (42.5-81.0)       | 69.0 (58.0-82.0)          | 0.0704              |
| Global Vas(0-100)                                       | 65.0 (43.5-81.0)       | 69.0 (49.5-79.0)          | 0.2209              |
| Joint Vas(0-100)  | 58.0 (43.5-78.5)       | 67.5 (51.0-80.0)          | <b>0.0375</b>       |
| Skin Vas(0-100)   | 30.5 (12.0-62.8)       | 33.0 (11.0-56.0)          | 0.8785              |
| PGA (0-5)   | 3.0 (2.0-4.0)          | 3.0 (3.0-4.0)             | <b>0.0049</b>       |
| Tender joint score (0-68)                               | 11.0 (5.0-20.0)        | 16.0 (11.0-25.0)          | <b>&lt;0.0001</b>   |
| Swollen joint count (0-66)                              | 5.0 (2.0-10.0)         | 7.0 (5.0- 12.0)           | <b>&lt;0.0001</b>   |
| CRP   | 6.0 (2.0-16.0)         | 8.5 (5.0-20.0)            | <b>0.0389</b>       |
| Absenteeism (%)<br>(n= 164 DMARDS, 65 anti TNF)         | 0.0 (149) 0.0- 8.1     | 0.00 (55) 0.0-9.2         | 0.7623              |
| Presenteeism (%)<br>(n= 164 DMARDS, 65 anti TNF)        | 30.0 (155) 10.0-60.0   | 40.0 (61) 20.0-60.0       | 0.3920              |
| Productivity Loss (%)<br>(n= 164 DMARDS, 65 anti TNF)   | 40.0 (150) 20.0-70.0   | 50.0 (55) 26.2-70.2       | 0.4906              |
| Activity Impairment (%)<br>(n= 164 DMARDS, 65 anti TNF) | 50.0 (163) 30.0-70.0   | 60.0 (65) 30.0-70.0       | <b>0.0259</b>       |

**Table 1- Baseline characteristics of 393 participants commencing DMARD or anti-TNF for active psoriatic arthritis**

Health Assessment Questionnaire (HAQ), European Quality of Life 5 Domain Index (EQ5D), Dermatology Life Quality Index (DLQI), Visual Analogue Scale (VAS), Patient Global Assessment (PGA), C-Reactive Protein (CRP), Disease Activity score Psoriatic Arthritis (DAPSA),

Seven patients did not commence a DMARD or anti-TNF and were excluded from the analysis.

Statistically significant differences between groups notified in bold

| Outcome<br>(range)                              | Baseline<br>Median (n)<br>IQR | 6 months<br>Median (n)<br>IQR | P value<br>(Wilcox) |
|---|-------------------------------|-------------------------------|---------------------|
| HAQ (0-3)                                       | 1.0 (236) 0.5-1.6             | 0.9 (198) 0.3-1.5             | 0.0643              |
| EQ5D (-0.11-1)                                  | 0.7 (238) 0.6- 0.9            | 0.8 (190) 0.7- 1.0            | <b>0.0243</b>       |
| DLQI (0-30)                                     | 2.0 (233) 1.0- 7.0            | 1.0 (188) 0.0- 3.0            | <b>&lt;0.0001</b>   |
| Pain Vas (0-100)                                | 62.0 (234) 42.0-81.0          | 45.5 (189) 23.8- 70.0         | <b>&lt;0.0001</b>   |
| Global Vas (0-100)                              | 65.0 (235) 43.3- 81.8         | 45.0 (189) 25.8- 69.3         | <b>&lt;0.0001</b>   |
| Joint Vas (0-100)                               | 57.0 (227) 42.3- 79.0         | 47.0 (186) 24.0- 67.0         | <b>&lt;0.0001</b>   |
| Skin Vas (0-100)                                | 32.0 (233) 12.0- 64.0         | 21.0 (186) 7.0-45.0           | <b>0.0009</b>       |
| Fatigue (0-52)                                  | 31.0 (232) 19.8-42.0          | 36.0 (188) 24.0-43.0          | <b>0.0189</b>       |
| Tender joint score (68)                         | 11.0 (268) 5.0- 21.0          | 7.0 (263) 3.0- 18.0           | <b>0.0005</b>       |
| Swollen joint count (66)                        | 5.0 (268) 2.0- 10.0           | 3.0 (263) 0.0- 7.0            | <b>&lt;0.0001</b>   |
| CRP (0->100)                                    | 0.6 (259) 0.2- 1.6            | 0.5 (242) 0.2- 1.0            | <b>0.0228</b>       |
| DAPSA   | 38.7 (n/a) 27.9-58.5          | 30.2 (n/a) 18.4- 48.5         | <b>&lt;0.0001</b>   |
| Absenteeism (%)<br>(164 working of 272)         | 0.0 (149) 0.0- 8.1            | 0.0 (145) 0.0-7.8             | 0.8751              |
| Presenteeism (%)<br>(164 working of 272)        | 30.0 (155) 10.0-60.0          | 20.0 (155) 10.0-42.5          | <b>0.0075</b>       |
| Productivity Loss (%)<br>(164 working of 272)   | 40.0 (150) 20.0-70.0          | 25.0 (144) 10.0-60.0          | <b>0.0147</b>       |
| Activity Impairment (%)<br>(164 working of 272) | 50.0 (163) 30.0-70.0          | 40.0 (163) 0.0-60.0           | <b>0.0036</b>       |

**Table 2- Clinical outcome of 272 participants commenced on DMARDS for active psoriatic arthritis**

Health Assessment Questionnaire (HAQ), European Quality of Life 5 Domain Index (EQ5D), Dermatology Life Quality Index (DLQI), Visual Analogue Scale (VAS), C-Reactive Protein (CRP), Disease Activity score Psoriatic Arthritis (DAPSA),

N= actual number of data before imputation

Statistically significant differences between groups notified in bold

| Outcome<br>(range)   | Baseline<br>Median (n) IQR | 6 months<br>Median (n) IQR | P value<br>(Wilcox) |
|--|----------------------------|----------------------------|---------------------|
| <b>HAQ (0-3)</b>   | 1.1 (101) 0.8-1.8          | 0.8 (80) 0. 0-1.4          | <b>0.0001</b>       |
| <b>EQ5D (-0.11-1)</b>  | 0.7 (102) 0.6-0.8          | 0.9 (82) 0.7- 1.0          | <b>0.0002</b>       |
| <b>DLQI (0-30)</b>   | 3.0 (97) 1.0-6.0           | 1.0 (79) 0.0-2.0           | <b>0.0002</b>       |
| <b>Pain Vas (0-100)</b>                                      | 69.0 (97) 57.5-82.0        | 33.0 (83) 11.0-57.0        | <b>&lt;0.0001</b>   |
| <b>Global Vas (0-100)</b>                                    | 69.0 (95) 50.0-79.0        | 31.0 (88) 12.0-60.0        | <b>&lt;0.0001</b>   |
| <b>Joint Vas (0-100)</b>                                     | 68.5 (86) 51.0-80.3        | 32.5 (82) 10.0-49.8        | <b>&lt;0.0001</b>   |
| <b>Skin Vas (0-100)</b>                                      | 33.0 (95) 12.0-56.0        | 14.0 (82) 40.0-26.0        | <b>&lt;0.0001</b>   |
| <b>FACIT (0-52)</b>  | 28.0 (86) 17.5-38.0)       | 38.0 (82) 25.0-46.0        | <b>&lt;0.0001</b>   |
| <b>Tender joint score (68)</b>                               | 16.0 (119) 11.0-25.0       | 4.0 (99) 1.0-14.0          | <b>&lt;0.0001</b>   |
| <b>Swollen joint count (66)</b>                              | 7.0 (119) 5.0-12.0         | 1.0 (99) 0.0-3.0           | <b>&lt;0.0001</b>   |
| <b>CRP(0-&gt;100)</b>  | 0.8 (116) 0.5-1.9          | 0.3 (89) 0.1-0.6           | <b>&lt;0.0001</b>   |
| <b>DAPSA</b>   | 52.8 (n/a) 38.3-66.4       | 14.0 (n/a) 6.9-37.4        | <b>&lt;0.0001</b>   |
| <b>Absenteeism (%)</b><br><b>(65 working of 121)</b>         | 0.0 (55) 0.0-9.2           | 0.0 (45) 0.0-0.0           | <b>0.0415</b>       |
| <b>Presenteeism (%)</b><br><b>(65 working of 121)</b>        | 40.0 (61) 20.0-60.0        | 10.0 (55) 0.0-30.0         | <b>&lt;0.0001</b>   |
| <b>Productivity Loss (%)</b><br><b>(65 working of 121)</b>   | 50.0 (55) 26.2-70.2        | 10.0 (45) 0.0-35.0         | <b>&lt;0.0001</b>   |
| <b>Activity Impairment (%)</b><br><b>(65 working of 121)</b> | 60.0 (65) 30.0-70.0        | 20.00 (55) 10.0- 50.0      | <b>&lt;0.0001</b>   |

**Table 3- Clinical outcome during follow up of 121 patients commenced on anti-TNF for active psoriatic arthritis**

Health Assessment Questionnaire (HAQ), European Quality of Life 5 Domain Index (EQ5D), Dermatology Life Quality Index (DLQI), Visual Analogue Scale (VAS), C-Reactive Protein (CRP), Disease Activity score Psoriatic Arthritis (DAPSA),  
N= actual number of data before imputation  
Statistically significant differences between groups notified in bold